EFFECTS OF THE INHALATION OF OXYGEN

BY L. B. BERGER AND S. J. DAVENPORT

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INTRODUCTION

Oxygen, because of its vital relationship to man's physical well being, is the most important chemical element. It may be breathed, however, only in a rather limited range of concentrations and pressures without producing ill effects. An excess of oxygen may be equally as harmful as too little of it. Because of the importance of these effects, the study of the physiological action of oxygen has received attention for many years and by many investigators. Much of the investigative work has been directed toward determining the limits within which oxygen in abnormal concentrations and at abnormal pressures may be breathed with safety in such applications as deep-sea diving, work in compressed-air, aviation, the wearing of apparatus designed to permit entrance into irrespirable atmospheres, and in the therapeutic applications of the medical profession.

The Bureau of Mines frequently receives requests for information on the effects of breathing essentially pure oxygen, because of the Bureau's association with the use of self-contained oxygen breathing apparatus for entering irrespirable mine atmospheres, and the use of oxygen in conjunction with artificial respiration as a means of resuscitation. The purpose of this paper is to summarize briefly the effects upon the human body of the inhalation of oxygen in various concentrations and at various pressures and to give reference to other published information that deals in greater detail with the diverse phases of the subject. The literature in this field is voluminous; therefore, a complete bibliography has not been presented in this paper. No paper on this subject would be complete without reference to the classic pioneering work of Paul Bert (1)[3/] in this field. Articles such as those of Stadie, Riggs, and Haugaard (2), Bean (3), Specht (4), and others cited contain extensive lists of references that will lead the reader to information in a degree of detail that is not within the scope of this publication.

MECHANISM OF RESPIRATION

As the effects of inhalation of oxygen under any condition of concentration or pressure have their inception through the process of respiration, that process is reviewed briefly to facilitate discussion of effects and actions that occur in the body subsequently to the initial intake of the oxygen-containing atmosphere. The mechanism and chemistry of the respiratory process are presented in detail in many text books of physiology (5) (6) (7) (8); the following are summarized statements from such sources.

The utilization of food and oxygen in the maintenance of life consists primarily of combustion processes. The essential elements of food are absorbed and carried by the blood to the body tissues where they are stored

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[3/] Numbers in parentheses indicate references in the bibliography appended to this paper.

as fuel for the production of heat and mechanical energy as required. Combustion or oxidation of this fuel supply is accomplished by oxygen carried by the blood stream from the lungs to the tissues where the combustion processes take place. Little or no oxidation occurs in the lungs or blood. Carbon dioxide that results from combustion or oxidation in the tissues is carried thence by the blood to the lungs, from which it is exhaled as a waste product. The transport of both oxygen and carbon dioxide by the blood is accomplished by readily reversible chemical reactions, in which the hemoglobin of the blood is involved, but in distinctly different ways for the transport of the two gases.

As in any combustion process, the rate at which energy may be produced by the body is dependent on the rate at which fuel is burned, which, in turn, requires that the rate at which oxygen is supplied be increased as energy is required. Thus, upon physical exertion the rate of respiration must be increased, and, as fuel is burned at a more rapid rate, the rate of production of carbon dioxide increases also. It is the concentration (tension) of carbon dioxide in the blood stream that regulates the rate of respiration by acting upon the respiratory nerve center in the brain. As the tension of carbon dioxide in the blood tends to increase because of increased rate of combustion in the tissues, the respiratory center is stimulated, and rate of respiration (or lung ventilation) is increased automatically, with the result that the concentration of carbon dioxide in the lungs is reduced proportionately. When the degree or extent of physical exertion is decreased, the carbon dioxide content of the blood tends to decrease, and the respiratory center again acts to decrease the rate of lung ventilation. This regulatory mechanism functions to maintain an essentially constant tension of carbon dioxide in the arterial blood and in the air in the alveolar spaces of the lungs by varying the rate of lung ventilation or oxygen intake to meet the energy requirements of the body.

The oxygen requirement of the body also is accommodated through the respiratory center of the brain, although in a somewhat different manner. Carbon dioxide acts directly upon this center, but the demand for oxygen is exerted first upon the carotid sinus, a small bulb on the carotid artery of the neck, which communicates through nerves with the respiratory center of the brain. In contrast to carbon dioxide, oxygen produces a stimulus of the respiratory center only when the body requires an augmented supply of oxygen. An excess of oxygen in the lungs does not tend to change the respiratory rate. If a normal man inhales pure oxygen instead of air, neither his breathing nor the consumption of oxygen by his body are increased markedly. In fact, the effect of inhalation of high concentrations of oxygen on metabolism (chemical changes that occur in the functioning of living tissue) appears somewhat controversial (2) (3). The fact that the rate of oxygen consumption does not increase significantly under this condition refutes the early theory that pure oxygen might not be breathed without danger of "burning up" the body through excessively rapid oxidation.

The control of respiration exerted through the carotid sinus comes into play only when, through vigorous physical effort, oxygen is consumed in the tissues more rapidly than it can be transported by the blood from the lungs to the tissues, or when an atmosphere deficient in oxygen is inhaled. Thus, under normal conditions of physical activity, and when breathing atmospheres of normal oxygen content, carbon dioxide in the tissues and blood stream exerts the chief and immediate control over rate of respiration (lung ventilation).

The complete mechanism of respiration is not as simple as set forth in the preceding paragraphs. Other factors, such as blood chemistry, the modes of transportation of oxygen and carbon dioxide by the blood, and the significance of the hydrogen-ion concentration of the blood, are not within the scope of this publication.

SIGNIFICANCE OF PARTIAL PRESSURE

The specific physiological effects produced by inhalation of a gas may be expressed by relating the nature or degree of effect to a certain concentration of the gas designated on a volume basis. Thus, it may be said that air containing 0.01 percent by volume of a certain gas may be breathed for 8 hours without ill effects, or that 500 parts of the gas per million parts of air may be dangerous to life for even a short exposure. Such terminology is used generally in defining the so-called "maximum allowable concentrations" of gases and vapors that may be encountered in various enviroments and in most circumstances is an adequate form of expression.

It must be recognized, however, that the entrance of a gas from the lungs into the blood and body tissues is governed largely by the partial pressure of that gas in the air or other mixture of gases inhaled. Partial pressure of a single gas in a mixture of gases is defined as the product of the concentration of that gas, on a volume basis, multiplied by the existing absolute pressure. For example, in normal air containing about 21 percent by volume of oxygen and 79 percent by volume of nitrogen (and other inert gases), the partial pressure of the oxygen at sea level, with a barometric pressure of 760 mm. of mercury, is

$$0.21 \times 760, \text{ or } 159.6 \text{ mm.},$$

and the partial pressure of the nitrogen is

$$0.79 \times 760, \text{ or } 600.4 \text{ mm.}$$

In contrast, if one were at an altitude of 5,000 feet above sea level, where the barometer registers about 630 mm. pressure, the partial pressure of oxygen in the atmosphere would be

$$0.21 \times 630, \text{ or } 132.3 \text{ mm.}$$

Thus, although the oxygen content of the atmosphere is constant at 21 percent by volume both at sea level and at an altitude of 5,000 feet, the partial pressure of oxygen in the atmosphere at the higher altitude is decreased markedly.

As gases such as oxygen are taken into the body mainly by solution and diffusion through the moist membranes of the lungs, the significance of partial pressure is evident, because the volume of a gas dissolved in a liquid, at a given temperature, is proportional to the partial pressure of that gas acting upon the liquid. Thus, for a given volume of air inhaled into the lungs, a smaller quantity (weight) of oxygen will enter the body for its vital functions at the lower barometric pressure existing at 5,000 feet altitude than at sea level, although the percentage composition of the air is the same at both locations.

Conversely, breathing air (approximately 1/5 oxygen by volume) at an absolute pressure of five times atmospheric (5 atmospheres) would have the same effect, insofar as oxygen is concerned, as breathing pure oxygen at a pressure of 1 atmosphere.

To illustrate further the principle of partial pressure: A man could not survive in an atmosphere containing only 5 percent of oxygen at atmospheric pressure, but if the pressure were increased to 4 atmospheres, the partial pressure of oxygen would be essentially that of normal air, and life could be maintained, insofar as oxygen requirements are concerned.

In considering and discussing the effects of the inhalation of oxygen, particularly at pressures greater than 1 atmosphere, it is convenient to designate the concentration of oxygen in terms of atmospheres partial pressure rather than as percent by volume. Thus, pure oxygen (100 percent) at a pressure of 1 atmosphere may be designated at "1 atmosphere of oxygen;" pure oxygen at a pressure of 2 atmospheres may be designated as "2 atmospheres of oxygen," rather than by the confusing term of "200 percent oxygen;" and normal air at atmospheric pressure may be considered as representing approximately 0.21 atmosphere of oxygen.

EFFECTS OF INCREASED OXYGEN CONCENTRATION AT ATMOSPHERIC PRESSURE

Considerable experimental work has been done on the effects of breathing oxygen in various concentrations in excess of that of normal air, and, as usual in such investigative work, there is some divergence in the conclusions reached. Reviews of the work such as those of Bean (3) and of Stadie, Riggs, and Haugaard (2) evaluate the findings of the various investigators and permit defining the effects in their general aspects, at least.

On the basis of these reviews it may be concluded that breathing increased concentrations of oxygen up to 100 percent at atmospheric pressure, (a) has slight or possibly no effect upon the oxidation processes in the body tissues, (b) no significant change in respiration is caused, and (c) prolonged exposure to high concentrations of oxygen results in irritation of the lungs and other pulmonary sequelae.

The severity of effects of breathing oxygen in concentrations that may cause symptoms is a function of the duration of exposure as well as the concentration of oxygen. Stadie, Riggs, and Haugaard (2), on the basis of findings of many investigators, conclude that oxygen at atmospheric pressure and in a concentration of 60 percent by volume (0.6 atmosphere) may be breathed "indefinitely" without ill effects, and that 99 to 100 percent (0.99 to 1.0 atmosphere) oxygen may be inhaled for 24 hours without producing symptoms. It must be noted that considerable variation exists in the opinions of the cited investigators in regard to the effects of pure oxygen, as the suggested safe exposures range from 7 to 40 hours. Consideration of the literature on the subject, however, indicates that with increasing knowledge of the subject the trend is toward acceptance of the higher limit rather than the lower.

EFFECTS OF OXYGEN AT PRESSURES GREATER THAN ATMOSPHERIC

Although the effects of increased concentration of oxygen at atmospheric pressure are characterized mainly by lung irritation and other pulmonary involvements, inhalation of oxygen at higher pressures produce symptoms of the central nervous system. At pressures of oxygen greater than 2 atmospheres the effects on the central nervous system are said to predominate (2). Symptoms of oxygen poisoning produced by high partial pressures of oxygen are convulsive seizures of the head, neck, and limbs, irregular and labored breathing, nausea, and in some cases apnea, or complete temporary cessation of breathing.

Behnke, Forbes, and Motley (9) studied the effects upon men of oxygen at pressures up to 3 atmospheres and observed dizziness, mental confusion or stupefaction, and changes in vision. Symptoms during the first 3 hours of such exposure are described as not distressing, but during the fourth hour severe and sometimes alarming symptoms occurred, including dizziness, nausea, and mental distress, although consciousness was retained.

Behnke, Johnson, Poppen, and Motley (10) observed that men breathing oxygen at a pressure of 4 atmospheres were affected by violent symptoms after approximately 45 minutes' exposure. At this pressure, convulsions or fainting may occur.

Griffith and Schrenk (11) describe the wearing for experimental purposes, of self-contained oxygen breathing apparatus (which supplied essentially pure oxygen to the wearer at the same pressure as that of the ambient atmosphere) in a sub-aqueous tunnel under construction, in which air pressure was maintained at a gage pressure of 36 pounds per square inch, or about 3.5 atmospheres absolute. In one experiment the subject, who exercised vigorously, experienced complete temporary cessation of breathing after 31 minutes, and, in a second experiment, violent increases in rate and force of respiration, followed by nausea, in 36 minutes.

Haldane (12) describes a feeling of terror after recovery from convulsive seizures induced in himself by exposure to oxygen at high pressure and concludes that with a pressure of 7 atmospheres of oxygen 5 minutes is about the limit of human tolerance.

Various other systemic effects are described and discussed in detail in the reviews previously cited (2) (3).

Stadie, Riggs, and Haugaard (2), in summarizing the findings of many investigators, present the following data on oxygen pressure and duration of inhalation that may be tolerated by man without development of symptoms:

Oxygen pressure, atmospheres	Time limit for man without development of symptoms, hours
1	7 to 40
2	0.75 to 3
3	0.5 to 2
4	0.2 to 0.7
7	0.1
9	0.05

The presence of carbon dioxide associated with oxygen at elevated pressure causes more pronounced effects than oxygen alone (13), although it appears controversial whether the carbon dioxide enhances the effects of the oxygen, or vice versa (2). Nitrogen associated with oxygen is apparently without effect as regards the symptoms of oxygen poisoning.

EFFECTS OF AIR AT INCREASED PRESSURE

Exposure to the effects of air at pressures greater than atmospheric is confined chiefly to diving operations and to work carried on in caissons or in under-water tunneling where the hydrostatic pressure of the surrounding water, or water-bearing stratum, is balanced by the pressure of compressed air to provide space and a habitable environment for those engaged in the work. The greater pressures are encountered in deep-sea diving, and consequently the greater hazards with respect to the effects of exposure to compressed-air, are associated with diving, although the physiological factors involved are similar in all phases of compressed-air work.

Each foot of depth below the surface of fresh water exerts a pressure of 0.4335 pound per square inch (about 0.446 in sea water). For work at any given depth, air must be supplied at sufficient pressure to balance the pressure of the water at that depth. Thus, in diving in fresh water to a depth of 100 feet, the gage pressure would be 100 x 0.4335 or 43.35 pounds per square inch; consequently, air must be supplied to the diver at this pressure. As the atmosphere exerts its normal pressure of 14.7 pounds per square inch upon the surface of the water, the total (absolute) air pressure to which the diver would be exposed is 43.35 + 14.7, or 58.05 pounds per square inch. Expressed in atmospheres, this pressure is $\frac{58.05}{14.7}$, or 3.95. As the air contains about 21 percent by volume of oxygen, the partial pressure of oxygen to which the diver would be exposed is 0.21 x 3.95, or 0.83 atmosphere.

It is evident, therefore, that in deep diving the effects of high partial pressure of oxygen must be considered. For example, in dives with compressed air to a depth of 300 feet, which have been accomplished, the partial pressure of oxygen to which the diver is exposed exceeds 2 atmospheres, which, as discussed in a preceding section, may induce lung irritation on fairly short exposure. To avoid this effect, synthetic mixtures of gases of lower oxygen content than normal air have been used in diving to great depths.

In diving, the effects of accumulation of carbon dioxide exhaled by the diver must be considered also, because the partial pressure and physiological effects of this gas increase as air pressure is increased. Thus, at atmospheric pressure an accumulation of 2 percent of carbon dioxide in the diver's helmet would have no marked effect upon him, whereas at an air pressure (absolute) of 5 atmospheres, or the equivalent of diving to a depth of 135 feet, the effects of this percentage of carbon dioxide would be the same as 10 percent of this gas at atmospheric pressure, which would produce serious symptoms in a short time (14).

Hill (15) states, in regard to the rate of air supply required by a diver to prevent effects from carbon dioxide, that "whatever the pressure a diver is under, he requires the same volume of air measured at that pressure." Hill states further that a diver at work must be supplied with at least 1.5 cubic foot of air per minute at whatever pressure he may be, and that a greater volume is to be preferred to maintain the carbon dioxide in the diver's helmet at a safe level. The above figure is a significant one in considering the delivery of air pumps or compressors to determine their adequacy for proposed diving operations.

Although the effects of partial pressure of oxygen and carbon dioxide in compressed-air work are significant, the most important effect is that of the nitrogen of the air. The body fluids and tissues are capable of dissolving nitrogen, and, as pointed out in a previous section, the extent of this solution is proportional to the partial pressure of the nitrogen. Thus, as a worker in compressed-air is subjected to increased air pressure the nitrogen of the air dissolves in his body, and the quantity of nitrogen dissolved is dependent on the pressure and the duration of exposure to that pressure. The effects of the solution of nitrogen may become evident when the worker is "decompressed" to atmospheric pressure. Under proper decompression the dissolved nitrogen is transported by the blood from the tissues to the lungs, whence it is exhaled, or it may diffuse harmlessly through the skin; but if decompression is too rapid, the nitrogen will form bubbles, or gas emboli, in the blood stream and in body tissues, resulting in symptoms such as pain in the joints, paralysis, and, in severe cases, death. Detailed discussion of the symptomatology and pathology of caisson illness, or the "bends," is not within the scope of this paper; the subject is covered thoroughly by other publications (3) (6) (12) (15) (16) (17) (63).

An additional action attributed to the solution of nitrogen in the body under compressed-air is a "narcotic" effect (18) (19), which results in aberrations in mental response and behavior. This effect is not accepted by others (3) as being attributable solely to nitrogen, but there seems no question, on the basis of experimental and practical observations, that such effect exists, whatever its exact cause may be.

In caisson work and sub-aqueous tunneling, where men often must undergo vigorous physical exertion in compressed-air, the effects of the solution of nitrogen in their bodies is of chief significance, because working pressures usually are not high enough to induce the poisoning effects of increased partial pressure of oxygen, and under most conditions the accumulation of carbon dioxide does not present a problem (20).

The extent of solution of nitrogen in the body, and therefore the possibility of experiencing the "bends" (caisson illness), upon decompression, is related to both the pressure of the air and the duration of exposure to that pressure. To avoid, as far as possible, the incidence of caisson illness of workers in compressed air, tables of safe working times at various ranges of pressure have been developed. Levy (20) cites such tables, enacted into law in New York State (1920), as follows:

Air pressure, pounds per square inch, gage	Maximum permissible working time
More than atmospheric and less than 22.	8 hours in any 24 hours, with return to normal pressure for at least 30 minutes during the 8-hour period.
22 or over and less than 30.	6 hours in any 24 hours, with the 6 hours divided into two 3-hour periods separated by a least 1 hour at normal pressure.
30 or over and less than 35.	4 hours in any 24 hours, with the 4 hours divided into two 2-hour periods separated by at least 2 hours at normal pressure.
35 or over and less than 40.	3 hours in any 24 hours, with the 3 hours divided into two 1-1/2 hour periods separated by at least 3 hours at normal pressure.
40 or over and less than 45.	2 hours in any 24 hours, with the 2 hours divided into two 1-hour periods separated by at least 4 hours at normal pressure.
45 or over and less than 50.	90 minutes in any 24 hours, with the 90 minutes divided into two 45-minute periods separated by at least 5 hours at normal pressure.

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As the return to normal pressure after exposure to compressed air may not be accomplished too rapidly without danger of the formation of bubbles of nitrogen in the blood and body tissues, so-called "decompression schedules" have been developed to provide reasonable safety from caisson illness of workers in compressed air. Levy (20) cites the following provisions of the law of New York State (1920):

> A stage decompression shall be used in which a drop of one-half maximum gage pressure shall be at the rate of five pounds per minute. The remaining decompression shall be at a uniform rate, and the total time of decompression shall equal the time specified for the original maximum pressure.
>
> Where the air pressure is greater than normal and less than 15 pounds to the square inch, decompression shall be at the minimum rate of 3 pounds per minute.
>
> Where the air pressure is 15 or over and less than 20 pounds to the square inch, decompression shall be at the minimum rate of 2 pounds per minute.
>
> Where the air pressure is 20 pounds or over and less than 30 pounds to the square inch, decompression shall be at the minimum rate of 3 pounds every 2 minutes.
>
> Where the air pressure is 30 pounds or over to the square inch, decompression shall be at the minimum rate of a pound per minute.

The foregoing regulations are included to illustrate that the degree of pressure to which the person working in compressed air is exposed determines both the safe maximum exposure and the safe minimum time of decompression. Tables and schedules similar to the foregoing have been developed for diving operations (21). It is generally considered that during decompression the air pressure may be reduced by half without serious hazard from the development of bubbles of nitrogen in the body. Thus, a diver may be raised from the bottom in stages or stops, each of which is at such depth that the pressure is half that at the preceding stage. The diver remains at each stage for enough time to permit gradual release of the nitrogen from his body at that depth and corresponding pressure. Navy diving procedure (21)includes the requirement that the rate of ascent between stages shall not exceed 25 feet per minute.

In deep-sea diving the required time of decompression often is the limiting factor in determining the depth to which a dive may be made with reasonable safety. Because of the possible onset of bad weather and rough seas during a dive, it is evident that diving to great depth is accompanied by the hazard of complications that may arise during the long period of decompression.

Recognizing that greater depths might be reached in diving and that the hazards of diving to any depth might be reduced by shortening the time of decompression, several persons, 4/ independently and at about the same time, conceived the idea of using helium-oxygen mixtures rather than compressed air for deep diving. The idea possessed several attractive possibilities: (1) Because of its lower solubility, a smaller volume of helium would dissolve in the body at a given pressure and therefore would present a slighter possibility of formation of gas emboli, or bubbles, on decompression; (2) because of its lower density and greater molecular activity, helium should diffuse more rapidly than nitrogen through body tissues; and (3) the use of synthetic helium-oxygen mixtures instead of compressed air would permit adjustment of the oxygen content of the mixture to avoid oxygen poisoning by excessive partial pressures of oxygen. Experiments that substantiated these theories were conducted by the Bureau of Mines (22) (23) (24) (25). Later, Behnke and Yarbrough (26) demonstrated that the "narcotic" effect of exposure to helium-oxygen mixtures under pressure was less than that of air (or argon-oxygen mixtures). The practical value of helium-oxygen mixtures in deep diving has been demonstrated during rescue and recovery operations conducted after the sinking of the submarine U. S. S. "Squalus" (27) and in other operations (28).

EFFECT OF OXYGEN-DEFICIENT ATMOSPHERES

Persons may be subjected to the effects of atmospheres deficient in oxygen either by breathing gaseous mixtures that at normal pressure contain less than 20.93 percent by volume of oxygen, or by breathing air at reduced pressure, as at high altitudes, where the partial pressure of oxygen is reduced, although the oxygen concentration, on a percentage basis, is normal. Discussion in this section is confined to the first case; that is, the effects of atmospheres containing diminished percentages of oxygen at ordinary barometric pressures. Such atmospheres may be encountered in confined spaces, such as mines, wells, and holds of ships, where the oxygen content of the atmosphere may be reduced by chemical reaction with some substance present, by sorption, as on coal surfaces, or by displacement and dilution by other gases, such as methane or nitrogen, that may occur or emanate in the space.

Although some individual variations apparently exist in response to a given reduction of oxygen in the breathed atmosphere, the symptoms may be generalized without loss of emphasis. The first signs of anoxia (want of oxygen) are increased rate and depth of breathing and increased pulse rate. Progressive symptoms with decreasing concentrations of oxygen are increased respiration, impairment of judgment, emotional instability, irregular respiration, nausea, loss of ability to move, unconsciousness, and death. Such symptoms occur in sequence if a man is subjected rather slowly to progressively decreasing concentrations of oxygen. In some instances, men exposed accidentally to oxygen-deficient atmosphers have fallen and remained

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4/ See Yant, W. P., Ind. and Eng. Chem., news ed., vol. 5, Mar. 10, 1927, pp. 4-5, for discussion of the various claims to origination of the idea.

inert, unable to move, but semiconscious and, although realizing that death was imminent, not greatly concerned by their plight (6). In other situations where men suddenly have entered atmospheres containing little or no oxygen there are no warning symptoms, and loss of consciousness is immediate. Such men, if rescued and revived, have no recollection of the incident, their last recorded thought being of their actions while in a normal state.

The immediate effects of exposure to atmospheres deficient in oxygen may differ somewhat with the individual and will depend on the degree of physical activity and also on the rate at which the oxygen content of the atmosphere is diminished. The following data, based on the observations of several investigators, are representative of the effects of breathing atmospheres of less than normal oxygen content:

Oxygen concentration, percent by volume (at atmospheric pressure)	Observed effects upon man
17	Rate and depth of respiration increased slightly (29).
16 to 12	Volume of breathing increased, and pulse rate accelerated (6).
15	Dizziness, rapid heartbeat, headache (29).
15	With moderate exercise, slight shortness of breath and slightly more than normal respiration. Some persons may become dizzy and suffer from headache (30).
12	Under gradual reduction of oxygen content, respiration becomes perceptibly deeper (31).
10	Symptoms of dizziness, rapid heartbeat, and headache become more severe (29).
10	Respiration becomes deeper and lips bluish (31).
10	Respirations are distincly deeper and more frequent, even at rest. Lips have appearance of cyanosis. Most persons become dizzy and suffer from headache after prolonged exposure and may become unconscious with moderate exercise (30).
10 to 6	Nausea and vomiting; inability to move and loss of consciousness (6).
9	Unconsciousness (29).
8	Face assumes a leaden color, although distress is not great (31).
8	Face becomes leaden color; severity of all symptoms increases; moderate exercise may cause sudden collapse and unconsciousness (30).
7	Life endangered (29).

Oxygen concentration, percent by volume (at atmospheric pressure)	Observed effects upon man
7	Unconsciousness (32).
Less than 6	Respiration convulsive, followed by death (6).
6 to 5	Marked panting; clouding of senses; loss of power of limbs; probably would end sooner or later in death. Sudden efforts may lead to loss of consciousness (31).
3.5	Under some conditions men have remained conscious (29).
2 to 1	Loss of consciousness without warning in 40 to 50 seconds (31).

Under experimental conditions it has been shown (33) that animals subjected to atmospheres deficient in oxygen to the extent that asphyxia was produced suffered degenerative changes in nerve tissue that were quite similar to those produced by carbon monoxide asphyxia. If the analogy may be applied to humans, it may be concluded that severe or prolonged asphyxia resulting from exposure to atmospheres deficient in oxygen may result in serious mental or nervous sequelae ranging in severity from temporary to permanent effects or death (34).

Atmospheres deficient in oxygen often are associated with abnormal concentrations of carbon dioxide, which usually is present as a product of the oxidation reactions that caused lowering of the oxygen content of the atmosphere. Because of this frequent association of high carbon dioxide with low oxygen, the effects of exposure to carbon dioxide are discussed briefly, although not strictly within the subject limitations of this paper.

Forbes and Grove (29) state that 0.5 percent of carbon dioxide in normal air causes a slight increase in lung ventilation; if the air contains 2 percent carbon dioxide, lung ventilation will be increased about 50 percent; and if 3 percent carbon dioxide is breathed, 100 percent.

Consolazio and others (35) found that 5 percent carbon dioxide, with the oxygen content of the atmosphere reduced to 12 percent, is the limit of tolerance for healthy young men. Exposure to such atmosphere did not seriously impair the physical condition or efficiency of the subjects. Minor symptoms of headache, nasal congestion, and dryness of the throat disappeared rapidly upon return to normal air. Adequate tension of oxygen in the lungs, blood, and tissues was maintained because of the resulting increased rates of respiration and circulation.

Brown (14) studied the effect upon man of carbon dioxide in concentrations of 6 percent and higher, with the following findings:

Time of exposure, minutes		Carbon dioxide, percent by volume	Effects
Average1/	Maximum2/		
21	22	6.0	Considerable discomfort toward end of exposure, but not intolerable. Exposure could have been extended.
4.5	6	7.5	More severe than above, but not intolerable. Exposure could have been extended.
8	10	8.8	Approaching intolerable limit.
1.6	2.25	10.4	Close to intolerable limit; sense of impending collapse.
1.1	2	12.4	Close to intolerable limit; sense of impending collapse. (One subject lost consciousness.)

1/ Average for 3 to 7 subjects.
2/ Maximum for any one subject.

EFFECTS OF REDUCED ATMOSPHERIC PRESSURE AT HIGH ALTITUDES

The atmosphere surrounding the earth exerts a pressure of approximately 14.7 pounds per square inch upon the earth's surface at sea level. This pressure will support a column of mercury 760 millimeters (29.92 inches) in height. Because of the compressible nature of gases, the density of the atmosphere is greatest at the earth's surface, and the relationship of pressure to altitude (distance above the earth's surface) is not linear. Thus, at an altitude of 50,000 feet the barometric pressure is not one-half but only about one-third of that at 25,000 feet. The following data illustrate the relationship of altitude to atmospheric pressure and partial pressure of oxygen in the atmosphere at certain significant levels:

Altitude, feet	Atmospheric pressure or partial pressure of oxygen in the atmosphere, percent of sea-level value	Partial pressure of oxygen in the atmosphere, millimeters of mercury
0	100	159
5,000	83	132
10,000	70	111
18,000	50	79.5
33,500	25	39.7
40,0001/	18.4	29.2

1/ Approximate limit of flying without pressurized equipment.

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Although the oxygen content of the atmosphere, on a percent-by-volume basis, is constant at the altitudes cited in the foregoing tabulation, it may be noted that partial pressure of oxygen decreases rapidly with increasing altitude. It is this reduction of partial pressure of oxygen and its resultant production of oxygen want in the body that is directly responsible for the physiological effects experienced upon exposure to reduced atmospheric pressures. Secondary or associated effects, of equal importance in the final outcome of such exposure, are changes in the character of respiration, changes in content of carbon dioxide (the primary regulator of respiration) of the blood and alveolar air of the lungs, and alterations in blood chemistry (4) (5) (6) (7) (36).

Although individuals may differ considerably in their response to a given diminution of pressure or in regard to the altitude at which they become affected, as pointed out by various investigators (4) (6) (7), the mechanism by which symptoms are caused at high altitudes may be generalized as follows:

The oxygen want created in the body by low partial pressure of oxygen stimulates the respiratory center through the carotid sinus, and the rate of respiration is increased. This rapid breathing reduces or "washes out" the carbon dioxide content of the blood and alveolar spaces of the lungs to a subnormal degree, and, when oxygen want has been relieved momentarily by excessive lung ventilation, the normal stimulus from carbon dioxide does not exist and the rate of respiration tends to decrease. Thus, respiration of a fluctuating nature, induced only by oxygen want, is experienced, and the hemoglobin of the blood is not maintained at its normal and required degree of saturation with oxygen. The severity of symptoms depends on the extent to which the oxygen content of the hemoglobin is reduced.

The symptoms of exposure to the low atmospheric pressures of high altitude are irritability, breathlessness, muscular weakness, confusion, lack of coordination, rapid heart beat, nausea, and, if carried to the extreme, unconsciousness and death.

Generally, when breathing normal air at an altitude of 10,000 feet, the oxygen content of the hemoglobin is not maintained at the normal degree of saturation and symptoms are experienced. Variations may exist as to the exact altitude at which the onset of these symptoms occurs with different individuals and are said (6) to be caused by variation in sensitivity to the stimulus of oxygen want. At whatever altitude symptoms develop, however, the immediately previous rate of respiration has been such that the same partial pressure of oxygen exists in the lungs of all individuals at the onset of symptoms. That is, although there may be individual variations in rate and volume of respiration at different altitudes, when partial pressure of oxygen in the lungs and, consequently, oxygen content of the hemoglobin fall below a certain critical value, the same symptoms will occur in all individuals (6).

The ill effects of breathing normal air at high altitudes may be alleviated by breathing pure oxygen or oxygen-enriched air, as under these circumstances rate of respiration is not increased by oxygen want, carbon dioxide is not washed out of the blood and alveolar spaces of the lungs, respiration remains normal, and higher altitudes may be attained without distress or ill effects. Another "ceiling" is reached, however, at between 40,000 and 45,000 feet above sea level, because at such altitudes even the breathing of pure oxygen at the existing atmospheric pressure does not suffice to maintain the oxygen content of the hemoglobin of the blood at its normal value. Specht (4) states that at 41,500 feet altitude, where atmospheric pressure is 132 millimeters, the carbon dioxide content or tension of the atmosphere in the lungs is 40 mm., [5] the tension of water vapor in the lungs is 47 mm., and the partial pressure of oxygen can be no more than 132-(40 + 47), or 45 mm., which will not maintain the oxygen saturation of the hemoglobin at more than 80 percent of its normal value - a condition that will be marked by the onset of symptoms.

The effects of ascending to high altitudes are influenced, also, by such factors as rate of ascent and duration of exposure to low atmospheric pressure. These effects may be considered in three categories:

1. The aviator who is piloting a fighter or pursuit plane capable of rates-of-climb of 5,000 feet, or more, per minute is subject not only to the effects of altitude when the ascent is accomplished but also to the effects of rapid decrease of pressure similar to the decompression of the diver or caisson worker who is returned to normal atmospheric pressure after being subjected to increased air pressure. The rapid release of dissolved nitrogen from the blood and body tissues under the condition of sudden decrease of pressure may bring on the same effects as the "bends" experienced by the compressed-air worker (4).

2. The aviator flying at high altitude, or the person who engages occasionally in mountain climbing, may be considered as individuals who have been transported from their normal habitat to a foreign environment to which they cannot become adjusted immediately. In consequence, ill effects are suffered.

3. Persons who live permanently at high altitudes undergo physical alterations or acclimatization that permits them to exist normally at altitudes that would cause distress or incapacitation to persons brought suddenly to the same condition of low atmospheric pressure (4) (5) (6) (7) (36). Acclimatization to life at high altitude is accompanied by permanent increase in the rate and volume of respiration, and an increase in the red blood cells and their hemoglobin content to facilitate transport of oxygen by the blood to the tissues. Adjustments in blood chemistry occur also, which result in a lowered normal tension of carbon dioxide in the blood and alveolar spaces of the lungs, so that the respiratory center maintains control of respiration in the acclimatized individual, whereas

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[5] In temporary ascents to high altitude, the carbon dioxide tension in the lungs and blood, if not washed out by rapid respiration, remains essentially constant at this value.

these not thus conditioned to high altitude suffer through loss or improper functioning of this control.

It is not within the scope of this paper to discuss in detail the physiological processes involved in exposure to the low atmospheric pressures associated with high altitudes; the references cited contain extensive discussions of the subject. Remedial measures that have been adopted for the effects of high-altitude flying are described in a subsequent section of this publication.

APPLICATIONS OF THE INHALATION OF OXYGEN

Self-Contained Oxygen Breathing Apparatus

Self-contained oxygen breathing apparatus has been used successfully for many years to provide protection when irrespirable atmospheres must be entered in mines and elsewhere. The historical aspects of the development and use of this type of equipment are presented in publications of the Bureau of Mines and others (7) (37) (38) (39).

The chief advantage of self-contained apparatus is that the wearer carries his own supply of oxygen for breathing, and thus may enter atmospheres that contain high concentrations of toxic gases and little or no oxygen. In this respect, the self-contained apparatus is superior to the gas mask, which is designed to filter toxic gases, in limited concentration, from atmospheres otherwise respirable with respect to oxygen content, but does not afford protection against atmospheres deficient in oxygen. The oxygen content of the atmosphere within the self-contained apparatus, 80 percent or more, if breathed at normal atmospheric pressure, will not harm the wearer, even though the apparatus is used during several successive 2-hour periods. (See section on EFFECTS OF INCREASED OXYGEN CONCENTRATION AT ATMOSPHERIC PRESSURE.) There are however, certain conditions under which oxygen breathing apparatus may not be worn with safety:

1. The apparatus may not be worn in atmospheres that contain contaminants that are corrosive to the skin or that may be absorbed through the skin in harmful amount. For example, high concentrations of ammonia will cause injury to the skin, and hydrogen cyanide will be absorbed through it with serious effects.

2. Certain vapors, such as gasoline, may permeate rubber parts of the apparatus if it is worn for excessively prolonged periods or is used in such vapors on successive occasions.

3. Self-contained apparatus that supplies the wearer with pure, or nearly pure, oxygen may not be used at pressures much above that of the normal atmosphere (14.7 pounds per square inch absolute) without danger of oxygen poisoning from the resulting high partial pressure of oxygen (11), as the apparatus supplies the wearer with oxygen at essentially the same pressure as that of the atmosphere surrounding him.

Self-contained oxygen breathing apparatus differs in design and operating principle, as described briefly in the following sections:

Closed-Circuit Regenerating Type Using Compressed Oxygen

This type of breathing apparatus was the first to be developed and still is considered the most satisfactory, particularly in mine rescue or recovery operations in which conditions may necessitate that the apparatus be worn continuously for 1 to 2 hours. The high-pressure supply of oxygen is contained in a steel cylinder, from which it is fed through suitable reducing and admission valves, and as required by the wearer, into a flexible reservoir or "breathing bag", from which the wearer inhales through a mouthpiece. Upon exhalation, the expired breath is directed through a granular alkaline material that removes the carbon dioxide discharged from the wearer's lungs, and the unconsumed oxygen is returned to the breathing bag, which is replenished with oxygen from the supply cylinder as required.

The purity of oxygen used in the closed-circuit breathing apparatus is important, as inert gaseous impurities tend to accumulate within the apparatus. The Bureau of Mines specifies that oxygen for this purpose shall contain at least 98 percent oxygen, no hydrogen, and not more than 2 percent nitrogen.6/ Oxygen produced by distillation of liquid air usually conforms to those specifications. Oxygen produced by electrolysis of water may contain an appreciable amount of hydrogen and is not recommended for use in closed-circuit breathing apparatus because of the possibility that explosive mixtures of hydrogen and oxygen might accumulate within the apparatus.

In ordinary use of the closed-circuit breathing apparatus, the air originally contained in the interior of the apparatus must be expelled by inhaling from the apparatus and exhaling to the outside, so that the nitrogen content of the original air is replaced by essentially pure oxygen. This procedure is necessary because the nitrogen impurity in the oxygen will accumulate in the apparatus, and if the original content of atmospheric nitrogen is not flushed from the apparatus at the start of wearing, dangerous reduction of the oxygen content of the closed system will result eventually. Accumulations of nitrogen7/ must be discharged from the apparatus by exhaling to the outside through a saliva-trap valve at intervals during the period of wearing.

6/ Analysis by the Bureau of Mines of the contents of several cylinders of oxygen produced from liquid air indicated that the "nitrogen" impurity consists of approximately equal proportions of nitrogen and argon. As argon is physiologically inert, it's behavior is similar to that of nitrogen in the breathing apparatus.

7/ In addition to nitrogen that will accumulate in the apparatus from the oxygen supply, some nitrogen from the wearer's body is added, because dissolved nitrogen in the blood and tissues will be liberated through the lungs when an abnormally high partial pressure of oxygen is established in the lungs. See sections on SIGNIFICANCE OF PARTIAL PRESSURE and EFFECTS OF AIR AT INCREASED PRESSURE.

Self-contained oxygen breathing apparatus of the closed-circuit, regenerating type is described in detail in other Bureau of Mines publications (37) (38).

Demand-Type Breathing Apparatus Using Compressed Oxygen

A "demand-type" breathing apparatus has been developed in which the high-pressure oxygen supply is contained in a steel cylinder, from which it is fed, through a suitable reducing valve, to the demand valve and thence to a full facepiece similar to that of a gas mask. The demand valve is actuated by the slight negative pressure induced in the facepiece by the wearer's inhalation, and supplies him with oxygen in proportion to the depth of his respiration. Exhaled oxygen is expelled from the facepiece to the outside through an exhalation valve. Some oxygen is wasted by this procedure, and although the apparatus is considerably lighter in weight than the closed-circuit type, its higher rate of oxygen consumption does not permit its use for as long as the latter.

The demand-type apparatus is described in greater detail in other Bureau of Mines publication (38) (40).

Chemical or Oxygen-Generating Breathing Apparatus

A closed-circuit breathing apparatus has been developed in which the oxygen supply is derived through the action of the moisture in the exhaled breath upon potassium tetroxide, according to the reaction

$$2K_2O_4 + 2H_2O \longrightarrow 4KOH + 3O_2$$

The carbon dioxide content of the exhaled breath is absorbed from the system by the potassium hydroxide formed in the above reaction. The rate of evolution of oxygen is governed by the rate of respiration of the wearer.

The apparatus comprises a replaceable canister that contains the chemical, a breathing bag to provide volume capacity in the apparatus, a full facepiece similar to that of a gas mask, suitable connecting tubes, and unidirectional valves to direct the flow of inhaled and exhaled air through the proper course in the apparatus. Although the apparatus is of a closed-circuit type, flushing of the initial air from it is not necessary, because ordinarily more oxygen is generated than is consumed, and excess oxygen usually excapes around the edges of the facepiece.

The oxygen-generating breathing apparatus is described in greater detail in other Bureau of Mines publications (38) (40).

Liquid Oxygen Breathing Apparatus

Apparatus utilizing the gasification of liquid oxygen to supply the wearer with a breathing medium has been developed and used to a limited extent in England but has not been adopted in the United States.

The difficulties of obtaining, storing, handling, and controlling the gasification of liquid oxygen are obvious disadvantages associated with this type of apparatus.

The liquid oxygen type of breathing apparatus is discussed briefly in other publications (37) (38) (39).

Self-contained oxygen breathing apparatus of the closed-circuit regenerating and demand types which utilize compressed oxygen, and the chemical or oxygen-generating type have been tested and approved by the Bureau of Mines under the provisions of appropriate Schedules of approval requirements (41). The approved devices are listed and described in publications of the Bureau of Mines (37) (38) (40) (42).

Bureau of Mines publications describe the maintenance and testing of self-contained oxygen breathing apparatus and contain instructions for its use and training in its use (37) (40) (43). These publications stress the importance of physical fitness of wearers of the apparatus, thorough training in procedure, and proper maintenance of the equipment. It is pointed out that accidents or loss of life during wearing of breathing apparatus have been due almost invariably to poorly assembled or otherwise defective apparatus, poor physical condition of the wearer, or insufficient training or some incorrect procedure (40) (44).

Use of Oxygen in Resuscitation and Treatment of Asphyxia

Asphyxia is defined by Henderson (7) as "process that occurs whenever it becomes difficult for the tissues to obtain the normal supply of oxygen." This concise statement describes a condition that may result from many causes, such as inhalation of toxic gases or atmospheres deficient in oxygen, electric shock, drowning, obstruction of the respiratory passages by foreign objects, and from other accidental happenings, the use of drugs and anesthetics, and from various diseases. A report of the American Medical Association (45) states that whatever the cause of asphyxia, "the basic problem in each case is reduced to the introduction of oxygen into the respiratory tract, the support of the center governing respiration, and stimulation of the circulation."

Asphyxia is a condition that may be encountered clinically by the physician or accidentally and in emergency by the layman, and therefore the immediate procedure that may, or should, be followed in its treatment will depend on the attendant circumstances. Moreover, the degree of asphyxia is to be considered. If normal breathing has not ceased, the layman should attempt only simple measures to better the condition of the affected person until medical aid is obtained, whereas if breathing has stopped, or is weak and intermittent, or is present only in occasional gasps, artificial respiration should be applied at once (38) (46).

An asphyxiated person suffers from deprivation of his oxygen supply; therefore, inhalation of pure oxygen will, in many instances, improve his condition. This is particularly true in cases of exposure to carbon monoxide, which produces its ill effects by combining with the hemoglobin of the blood with an affinity much greater than that of oxygen, thereby depriving the hemoglobin of its ability to transport oxygen to the body tissues. In carbon monoxide asphyxia the breathing of oxygen, rather than air, will hasten the dissociation of the carbon monoxide-hemoglobin complex through the effects of partial pressure and mass action, and will reduce the severity of the symptoms and decrease the possibility of serious after effects (47) (48).

Henderson and Haggard (49) suggested the administration of carbon-dioxide-oxygen mixtures in the treatment of carbon monoxide asphyxia instead of oxygen alone. Such mixtures, which contain 5 to 7 percent carbon dioxide and 95 to 93 percent oxygen, have been used widely in the treatment of asphyxia from various causes (7) (50). Experiments conducted by the Bureau of Mines (51) demonstrated that carbon monoxide is eliminated from the blood five to six times more rapidly when breathing carbon dioxide-oxygen mixtures than when breathing normal air, and that the elimination is accomplished about four times more rapidly when breathing pure oxygen than when breathing normal air.

There has been considerable controversy over the indiscriminate use of carbon dioxide-oxygen mixtures in treatment of asphyxia, and it has been pointed out (50) that in cases where the affected person is not suffering from want of carbon dioxide in his tissues, with its accompanying stimulus of the respiratory center, the administration of additional carbon dioxide may be more harmful than beneficial. Some of the benefits claimed for the administration of carbon dioxide-oxygen mixtures in asphyxia are as follows:

1. In cases of exposure to toxic or oxygen-deficient atmospheres or in cases causing shock or pain, the rate of breathing prior to collapse may have been so rapid as to wash out carbon dioxide from the system, thereby leaving the blood and tissue in need of carbon dioxide to stimulate the respiratory center and promote normal breathing.
2. In cases of carbon monoxide asphyxia, the lowered oxygen-carrying capacity of the blood reduces the extent of oxidation reactions in the tissues and thereby lowers their carbon dioxide content to less than normal, resulting in the need of additional carbon dioxide to produce respiratory stimulus.
3. In cases where carbon dioxide has been washed out of the blood and tissues by violent respiration prior to collapse, the administration of pure oxygen will satisfy the oxygen want of the body momentarily, but, in the absence of carbon dioxide in the body, to provide the normal respiratory stimulus, apnea or cessation of breathing may result, with serious effects unless respiration is maintained by artificial means.

In contrast, the following unfavorable opinions have been expressed (52) regarding the use of carbon dioxide-oxygen mixtures:

1. Although carbon dioxide-oxygen mixtures increase the depth of respiration when administered for a short time in low concentrations, this same effect is not exhibited when the centers of respiration are damaged, when the concentration of carbon dioxide is high, or when it is used over a prolonged period.

2. In asphyxiated persons, the blood oxygen concentration is almost nil, but the blood carbon dioxide level is above normal. In these persons carbon dioxide no longer acts as a respiratory stimulant but is actually a respiratory depressant, and there is no rational basis for its administration. The same may be said of cases of severe carbon monoxide poisoning, for medullary damage is present in all states of severe anoxia.

Eastman, Dunn, and Kreiselman (53) draw the following conclusions on the basis of animal experimentation as related to asphyxia in newborn infants:

1. When animals are asphyxiated to the state of apnea (cessation of breathing), resuscitation is accomplished just as quickly by the administration of pure oxygen as by use of carbon dioxide-oxygen mixtures; in profound asphyxia, pure oxygen is more efficacious than carbon dioxide-oxygen.

2. Following resuscitation with oxygen, the restored respiration remains normal in rate, amplitude, and general character, but following resuscitation with carbon dioxide-oxygen the respiration tends to be convulsive and irregular, and frequently becomes so shallow that further artificial respiration is needed.

The foregoing findings are based upon experiments with mixtures containing 10 and 25 percent carbon dioxide, or somewhat more than the 5 to 7 percent carbon dioxide-oxygen mixtures ordinarily used in resuscitation.

Flagg (50), in his book on resuscitation, although expressing himself as having found carbon dioxide-oxygen mixtures beneficial, sums up the situation in a logical manner by stating, in substance, that the use or non-use of carbon dioxide-oxygen mixtures in asphyxia should be determined by symptomatology rather than by adoption of a dogmatic point of view. Flagg states, in part, that "The objective in resuscitation is to saturate the alveolar air (of the lungs) with oxygen as quickly as possible. If spontaneous breathing can be deepened by carbon dioxide at the onset of resuscitation, this advantage may well balance the question of possible danger. The use or abuse of carbon dioxide is but one factor in the art of resuscitation. Any interference with the technical administration of oxygen would seem to be of greater importance than its dilution by another gas of whose action there is so much question."

Certain mechanical devices have been developed for the purpose of applying artificial respiration (38) (50). Some of these obtain lung ventilation by supplying the affected person with air or oxygen alternately under positive and negative pressure. The use of such devices by the layman is not recommended (6) (38), because it has been found that they do not conform to natural breathing, may injure lung tissue by excessive pressure and suction, and are dangerous.

In the treatment of poisoning by toxic gases or asphyxia produced by oxygen-deficient atmospheres, the Bureau of Mines recommends (38) that when the condition of the victim indicates need for artificial respiration, it should be applied preferably by the prone-pressure method. It is emphasized, also, that in cases of carbon monoxide poisoning inhalation of pure oxygen or oxygen containing 5 to 7 percent of carbon dioxide will be beneficial, and should be administered by use of an inhaler that supplies these gases to the victim at atmospheric pressure.[8]

Use of Oxygen to Prevent or Mitigate Compressed-Air Illness

Inhalation of oxygen to prevent or mitigate compressed-air illness was suggested many years ago (1) and more recently has been studied experimentally (15) (28) (54) (55) (56) (57) and applied in practice (27) (58). The basic principles of this use of oxygen are, briefly, as follows: Under ordinary conditions the body fluids and tissues contain dissolved nitrogen, being at equilibrium with the nitrogen content of normal air at atmospheric pressure. Changing the tension of nitrogen in the lungs by changing either the pressure or the nitrogen content of the respired atmosphere will alter the dissolved nitrogen content of the body through the effect of partial pressure.

The diver or compressed-air worker in an environment of air at pressures greater than 1 atmosphere attains in his body a dissolved nitrogen content in excess of that which exists at normal pressure, the quantity of nitrogen dissolved depending on pressure and duration of exposure. Upon returning to normal pressure or being "decompressed," a considerable part of this excess dissolved nitrogen is carried to the lungs by the blood stream and is exhaled. Compressed-air illness may result if bubbles of nitrogen, formed as a result of too rapid decompression, lodge in the body and are not dissipated through the lungs.

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[8] Bureau of Mines safety equipment includes inhalers charged with oxygen only, not carbon dioxide-oxygen mixtures. One reason for this standardization on oxygen is that it is more readily available because of its wide use in industry.

By breathing oxygen rather than air during decompression, the transition of dissolved nitrogen from the blood to the lungs is facilitated because of the lower partial pressure of nitrogen in the lungs. That is, when the lungs contain oxygen instead of normal air, the nitrogen dissolved in the blood encounters no "back pressure" of gaseous nitrogen in lungs and thus is freed from solution in the blood more readily and to a greater extent than if the lungs contained air. Moreover, if nitrogen bubbles form in the body, an arterial blood stream of low nitrogen content will tend to take these bubbles into solution much more readily than if the nitrogen content of the blood were that established by breathing air during decompression.

The limiting factors in the use of oxygen for inhalation during decompression are the pressure at which oxygen may be applied, and the duration of such application, without incurring the danger of oxygen poisoning.

In diving operations it has been shown (57) that oxygen may be supplied to the diver with safety at a depth of 60 feet (equivalent to 2.8 atmospheres pressure, absolute) and that breathing oxygen thereafter during stage decompression for 1-1/2 hours is without ill effect. By this procedure the safe time of decompression after dives to a depth of 165 feet, with a stay of 30 minutes at that depth, was reduced markedly, as compared to the time required if air were breathed throughout the total decompression operation.

In a subaqueous tunneling operation (58) workers were administered oxygen during the last 20 minutes of decompression at 15 to 17 pounds per square inch gage pressure after initial decompression from working pressures of 34 to 37-1/2 pounds per square inch. This procedure was followed throughout a 3-month period without ill effects from the inhalation of oxygen and with reduction in the incidence and severity of the symptoms of compressed-air illness.

Use of Oxygen in Aviation

Inhalation of oxygen in high concentration plays an important part in aviation (59) (60), by enabling continued flight at high altitude, conditioning the aviator for the effects of rapid ascent to the high altitude, and aiding his vision for night flying. These subjects are discussed briefly in this publication. Much work relating to the physiological aspects of aviation was carried out during World War II; numerous references to such work are cited by Specht (4). Aviation medicine is discussed by Armstrong (61), and a bibliography on the subject has been prepared by Hoff and Fulton (62).

The effects of decreased partial pressure of atmospheric oxygen experienced in flying may not be defined too precisely in terms of altitude alone, as some variation exists between individuals, and the effect of length of stay at a given altitude is important. In general, when breathing normal air at the existing ambient presure, the first appreciable symptoms may be experienced at 10,000 feet, because partial pressure of oxygen in the atmosphere at that height is not enough to maintain the normal degree of oxygen saturation of the hemoglobin of the blood. For unacclimatized persons the limit for air-breathing in aviation is 15,000 to 16,000 feet (4). The breathing of pure oxygen at the ambient pressure of the altitude of flight establishes a partial pressure of oxygen in the lungs that permits ascent to about 40,000 feet, where again a ceiling is reached because even the breathing of pure oxygen at the existing atmospheric pressure does not suffice to maintain normal saturation of the hemoglobin with oxygen.9/ Higher altitudes may be attained, with reasonable expectancy of survival, only by the use of aircraft with pressurized compartments for personnel or by wearing of pressurized flying suits. In general, it is recommended that inhalation of oxygen be started at 10,000 feet (4).

In night flying, the inhalation of oxygen is necessary for even low-level operations as it has been demonstrated that the ability of the eyes to adapt to night vision and the discernment of objects in night flying are reduced about one-half at altitudes of 10,000 to 12,000 feet if normal air is breathed (4).

The ascent of the aviator to high altitude, with the accompanying decrease of ambient pressure, is similar in effect to decompression of the diver or caisson worker after exposure to compressed air, (63). The decrease in pressure of the surrounding atmosphere causes liberation of nitrogen dissolved in the blood and body tissues at the preceding state of pressure, which, in the case of the aviator, is that of the atmosphere at ground level. If the rate of liberation of nitrogen is high enough, bubbles of this gas may be formed in the blood and tissues, with the resultant symptoms of "bends" or compressed-air illness.

The rate of ascent to high altitude and the altitude attained are the conditions critical to the development of symptoms of the bends in aviation. At rates of climb as great as 5,000 feet per minute, symptoms are developed, in general, only if flight is continued to heights of 18,000 to 20,000 feet (4) (17).

The effects of nitrogen liberation in the body resulting from rapid rates of ascent or flying at extreme altitude may be rduced or eliminated by inhalation of oxygen (4) (17) at ground level prior to flight. This procedure, by establishing a low or zero partial pressure of nitrogen in the lungs, results in elimination of dissolved nitrogen from the body, because this gas is dissipated from the blood stream in the absence of "back pressure" of gaseous nitrogen in the lungs. If the rate of climb of the aircraft is low, inhalation of oxygen from ground level during flight may be sufficient to eliminate body nitrogen to an extent that will prevent symptoms of the bends before critical altitudes are attained.

9/ See section on Effects of Reduced Atmospheric Pressure at High Altitudes.

It may be noted that oxygen poisoning is not generally a serious possibility in aviation, as pure oxygen is inhaled at pressures less than 1 atmosphere. Behnke (17) states that men may ascend at the rate of a mile a minute to 37,000 feet and exist normally at that altitude for 6 hours, provided dissolved body nitrogen is removed by oxygen inhalation at ground level or up to 20,000 feet.

Oxygen Therapy In General Medicine

The isolation of oxygen by Priestly in 1775 and the determination by Lavoisier, during 1775 to 1794, of the fundamental principles of breathing (64) opened the way for the discovery of the important role played by oxygen want in many diseases and physiological conditions and led finally to the increasing therapeutic use of oxygen in general medicine. Progress in oxygen therapy has at times been retarded by lack of confidence in its efficacy as a result of unsatisfactory reaction from delay in administering the treatment or inefficiency in applying the oxygen.

Paul Bort, in 1878 (65), was the first to point out that in the higher organisms the immediate cause of death of the body as a whole is virtually always want of oxygen, owing to failure of the circulation or breathing. This is due to the fact that the body has very little storage capacity and must depend from moment to moment on its supply from the air. The lungs offer almost the only appreciable storage space for oxygen. A man at rest, who has been breathing normally, can have his breathing interrupted for only about 1-1/4 minutes before urgent symptoms of oxygen want appear. When the supply of oxygen to the blood is shut off, the most "threatening symptoms" appear immediately (66).

Priestly, who failed to understand the significance of his discovery, is said (67) to have been the first to suggest that oxygen could be used to advantage therapeutically, although such use might be attended by some danger.

Beddoes (68) investigated the therapeutic value of oxygen, his research extending from 1793 to 1801. In 1800 he (64) established a pneumatic institute at Bristol, where he gave inhalation treatments for heart disease and asthma. However, his technique of administering oxygen was inadequate and did not result in the success that he had expected. Interest was not taken in oxygen again until 1917, when Barcroft (69) began treating gassed soldiers with 40 to 50 percent oxygen.

Thirty-five years ago no one had the temerity to suggest that a pneumonia patient be given oxygen to breathe (70). However, with Barcroft's (69) favorable report on the treatment of 23 cases of gassed soldiers, which appeared in 1920, and the development of better physiological methods of examination of such patients, impetus was given to other investigators, and reports on the effect of the administration of 40 to 60 percent oxygen in pneumonia soon followed (69).

Physiological Conditions In Which Oxygen Therapy Is Indicated

It is not practicable in this paper to refer to all the investigators who have studied the role of oxygen in animal and human organisms. Zuntz, Haldane, Barcroft, Krogh, Bohr, Van Slyke, Henderson, Campbell, and Poulton are a few of the many scientists who have provided additional insight into the mechanism of breathing (64).

In modern medical practice inhalation therapy is said (64) to be important in cardiac failure, congestive heart failure, coronary artery disease, asthma, atelectasis of the lungs of the newborn (imperfect expansion of the lungs at birth), postoperative atelectasis (partial collapse of the lungs), pneumonia, pulmonary edema (serous fluid in the air vesicals and tissues of the lungs), emphysema (swelling due to air in the tissues), anoxia and brain lesions following fever therapy, head injuries, paralysis of the pulmonary musculature, cerebral embolism (obstruction by a clot in an artery in the main part of the brain), chronic pulmonary tuberculosis, blast injuries of the lungs, aerial transportation of patients with miscellaneous diseases, submarine medicine and caisson disease, shock, accidental asphyxia, hemorrhage, peripheral arteriosclerosis (thickening of the coats of the arteries of the extremities), migraine (periodic nervous headache accompanied by nausea, vomiting, and various sensory disturbances), seasickness, gas gangrene and tetanus, and war-gas poisoning and lung irritants.

Types of Oxygen Want

There has been much discussion regarding the proper terms to express the condition of oxygen want in the body. Various suggestions have been made, mostly based on the word *anoxemia* which is derived from the Greek *an*, meaning privation, plus *oxygen* plus *emia* (73).

A general term, *anoxia*, which may be interpreted as oxygen want, has been suggested by Barcroft (73) to include all conditions of oxygen want in the body regardless of cause. He also suggested three types of anoxia to be recognized: "Anoxic", "anemic", and "stagnant." Peters and Van Slyke (73) have suggested a fourth, "histotoxic anoxia" (Greek *histo*, meaning *tissue*, and *toxikon*, meaning poison). The failure to distinguish between *anoxia* and *asphyxia*, which means literally "without pulse", has caused considerable confusion. Van Liere has suggested that *anoxia* be used to designate a diminished supply of oxygen to the tissues, and *asphyxia*, a condition of anoxia combined with an increase of carbon dioxide tension in the blood and tissues. This is based on Henderson and Haggard's (74) description of two forms of asphyxia. One form they described as caused by cessation of breathing, so that there is an excess of carbon dioxide in the body. This could be caused by anything that stopped respiration. As anoxia develops, the carbon dioxide accumulates, so that both conditions affect the body. In the other form they described, however, there is no interference with breathing except as a terminal event.

The classification of anoxia suggested by Barcroft and Peters and Van Slyke and quoted by Van Liere (73) is discussed in some detail below.

Anoxic anoxia

This is one of the most serious forms and affects the whole body. It may be produced by:

1. Low tension of oxygen in the inspired air as a result of exposure to high altitudes, anesthetic agents, or breathing inert gases.
2. Abnormal conditions within the lungs, such as the presence of fluid (caused by drowning) or from edema or exudates; obstruction of air passages by other than fluids; pneumonia; collapse of the lungs, emphysema.

3. Shallow respiratory movements from any cause.

4. Reflex inhibition of respiration from any cause (exposure to nonrespirable gases, blow on the solor plexus, etc.).

5. Embryological malformations of the heart or blood vessels.

During anoxic anoxia the partial pressure of oxygen and saturation of hemoglobin are both reduced. Reduction in arterial pressure is more important than the lack of oxygen saturation. Evidence is available (73) that the velocity of the oxidative processes in the tissues is proportional to the partial pressure which the oxygen exerts. Lowering of the partial pressure of the oxygen in the inspired air is therefore a serious handicap to the body.

Also, the increased respirations produced by anoxia wash the carbon dioxide out of the lungs, causing the carbon dioxide arterial pressure to fall. When the carbon dioxide tension is decreased, the hemoglobin does not give up its oxygen readily; consequently, the tissues suffer from oxygen want, although there may be adequate oxygen in the blood.

Anemic anoxia

Although this type is less serious than the anoxic type, it affects the whole body (73). This type may be caused by the following conditions:

1. Acute or chronic hemorrhage from any cause.
2. Primary or pernicious anema and secondary anemia or chlorosis.
3. Alterations in the hemoglobin from nitrites, chlorates, and coal-tar derivatives.
4. Carbon monoxide poisoning.

Stagnant anoxia

This type is due to a diminution in circulatory rate. Only local areas of the body may be affected or the whole body may be involved. This type may be produced by:

1. General failure of the circulation or by local failure, such as in Raynaud's disease (gangrene due to local asphyxia).
2. Impairment of venous return.
3. Shock.

Histotoxic anoxia

In this type of anoxia the cells are not able to utilize the oxygen, although the amount of oxygen in the blood may be normal and under normal tension. It is produced characteristically by cyanides but may be produced theoretically by any agent that depresses cellular respiration.

Treatment of Anoxia

The three chief groups of indications for oxygen administration are (1) to combat arterial anoxemia, (2) to hyperoxygenate the blood in conditions not associated with anoxemia (coronary occlusion, fever, migraine, polycythemia, and so on), and (3) to eliminate nitrogen from the body (to prevent decompression sickness or to combat intestinal distention) (72).

There is a great difference of opinion as to the amount of oxygen that should be administered under various conditions calling for oxygen therapy. According to Evans (69), no doubt thousands of lives could be saved each year by a better understanding of oxygen therapy. Its control is often of vital importance in many diseases and conditions in which anoxemia is frequently a serious complication.

Dosage

Forty to 60 percent oxygen has been considered by many to be the safe dosage. Others feel that up to 100 percent is necessary for best results. Evans (69) found that best results in pneumonia were obtained when 100 percent oxygen was given continuously from the beginning of the disease, whether or not cyanosis was present.

An ill patient is given additional opportunity to recover when administered oxygen to maintain respiration. In recent years it has been determined that certain tissues are more sensitive to oxygen want than others. The arms or legs may be deprived of oxygen for as long as 1-1/2 hours by complete closure of the arterial blood supply and yet will function normally afterward. On the other hand, a person may die when exposed to complete asphyxia for 10 minutes or less. The organ most sensitive to anoxia is the brain, where pathological changes appear in the cortical cells accompanied by hemorrhage as a result of asphyxia. The function of the heart also is quickly impaired when it is supplied oxygen at lowered pressure. The adrenal glands probably are quickly impaired by anoxia (64).

In general clinical medicine, it is not of great importance that a patient's vision or judgment is transiently impaired (64). However, in aviation the effects of oxygen want may imperil the lives of others as well as that of the one affected if he should be the pilot of an airplane. Barach (64) states that 40 percent oxygen is adequate to overcome altitude anoxia up to approximately 18,000 feet. For higher altitudes, the oxygen concentration may be increased to 100 percent, which protects the individual from anoxia up to 34,000 feet.

The effects of breathing high concentrations of oxygen have been studied intensively by many investigators on a variety of animals. Most of these investigators have reported the occurrence of irritation, congestion, and edema of the lungs, and even death following long exposure. As a result of the introduction and widespread use of apparatus designed to deliver 100 percent oxygen, Comroe, Dripps, Dumke, and Deming (72) conducted controlled experiments to determine the limits for safe oxygen usage in therapy and aviation. They reached the following conclusions:

1. One hundred percent oxygen administered to a large group of normal men continuously for 24 hours produced substernal distress in 82 percent. Vital capacity was usually decreased significantly. Signs of nose and throat irritation were common. Control subjects breathing room air through the same apparatus did not experience these symptoms.
2. Intermittence (up to 15 minutes rest every 3 hours) did not decrease the incidence of the complaints.
3. Seventy-five percent oxygen produced symptoms in only 55 percent of the subjects; 50 percent oxygen produced no symptoms during the 24-hour period. As oxygen tents or catheters rarely produce alveolar oxygen concentrations higher than 50 percent, these forms of administering oxygen are completely safe.
4. Breathing of 100 percent oxygen at high altitudes (low total atmospheric pressures) does not produce symptoms, indicating that the symptoms are due to high oxygen tensions and not to elimination of nitrogen.
5. The use of 100 percent oxygen for short periods is probably safe in all patients, but when oxygen must be given for more than 12 hours these rules should be followed: (a) The oxygen concentration should be reduced to 60 percent unless this is insufficient to saturate the arterial blood, and (b) if 100 percent oxygen must be administered a careful check should be made for the symptoms most likely to occur as a result of the high tension of oxygen.

Cullen and Skewis (71) mention the pulse rate as the most reliable sign of early oxygen want. As anoxia develops the pulse rate increases, and as it is relieved by excess oxygen the pulse returns to its original rate. If there is no change in the pulse rate with the administration of oxygen, it can be assumed that the tachycardia is not due to oxygen want. The pulse rate also can be used as a guide to the proper time for the discontinueance of oxygen therapy. If the oxygen is discontinued and the pulse rate rises, the patient still requires excess oxygen.

Central nervous system changes are manifested in early oxygen want. These are represented by sighing, yawning, and restlessness progressing at times to acute delirium. This restlessness, a common manifestation of oxygen want, too often is mistakenly treated with sedative drugs. The depressant action of these drugs only increases the oxygen want and fails to control the restlessness until dangerous doses are employed (71).

Precordial (over the heart or stomach) pain may develop with early oxygen want and some individuals will have fibrillary muscle twitchings. Cyanosis, which at first may have been only slight, may become marked, and convulsions may replace the twitchings (71).

A new method of treatment of silicosis and anthracosilicosis with intermittent positive-pressure breathing plus nebulization of bronchodilator drugs has been developed (75) for the treatment of patients with silicosis, emphysema, and dyspnea, with and without bronchial infection. More than 1,000 miners are said (76) to have been given similar treatment. All patients (72) received a course of treatment of 1 to 2 weeks' duration consisting of four 15-minute applications per day of intermittent positive-pressure breathing, using 100 percent oxygen and 1.5 cc. of 0.5 percent neosynephrine in the nebulizer. Secondary reactions have not been noted. Use of penicillin in concentrations as high as 50,000 units in 1.0 cc. of saline combined with aforementioned amount of neosynephrine in patients with superimposed bronchial infection has been satisfactory. All patients treated thus far have reported some subjective relief consisting primarily of less "tightness" of the chest, "lighter" and easier breathing, decreased secretions and cough, improved apetite, and more strength. In anthracosilicotic patients with dyspnea promotion of better drainage from the bronchi and bronchioles appears to be the most beneficial effect of the treatment.

The method of treatment using intermittent positive-pressure breathing obviously is not a cure for anthracosilicosis, but in about 60 percent of the advanced cases definite symptomatic relief can be expected when 100 percent oxygen is employed; improvement in function in the less severe types permits the miner to return to work. In the latter group, it has been found advisable to provide one treatment daily before or after work. Motley and coworkers discuss in more detail in the Archives of Industrial Hygiene and Occupational Medicine (77) the methods of determining the degree of disability (inability to work) that is the nature of the respiratory impairment in anthracosilicosis and the correlation of the results with the usual clinical findings, and the results of treatment with intermittent positive pressure breathing. They state:

In the attempt to provide subjective relief in patients with anthracosilicosis, the most effective treatment has been the simultaneous use of intermittent positive pressure breathing and nebulization of bronchodilator drugs (vapnefrin or isuprel). This treatment promotes bronchial drainage, provides a more uniform distribution of aerosols, with increased effectiveness of the bronchodilator drugs in relieving bronchospasm, and provides a breathing exercise improving muscle tone. The data obtained from physiologic studies with intermittent positive pressure breathing indicate that the increase in oxygen saturation of arterial blood and the decrease in the mean oxygen pressure gradient from alveoli to arterial blood in breathing air result from a more uniform aeration of alveoli in which the ventilation impaired by mechanical obstruction from fibrosis and loss of elasticity was further hampered by bronchospasm.

Methods And Apparatus For Therapeutic Administration of Oxygen

Inhalation

The first requirement for effective and economical administration of oxygen for therapeutic purposes is a supply of oxygen in large industrial-type cylinders of 200 cubic feet or more capacity. The former use of "medical" oxygen in low-pressure cylinders was expensive, wasteful, and difficult to regulate. However, to employ the oxygen available in large cylinders at high pressures, a dependable oxygen regulator is necessary with all types of oxygen-therapy equipment. Such a regulator, with directions for its use, is available (64).

Cullen and Skowis (71) mention five fundamental and practical criteria for evaluating the various modes of administering oxygen. The methods must be (1) clinically or scientifically officacious; (2) readily available for large numbers; (3) economical; (4) a simple technic; and (5) must not interfere with nursing care.

The methods of administering oxygen therapy commonly in use are: The oxygen tent, the mask, the oropharyngeal catheter, positive-pressure helmet apparatus, oxygen face tents and loose fitting masks, and oxygen chambers and oxygen rooms.

The oxygen tent is used to administer oxygen concentrations between 40 and 60 percent and to provide the patient with hygienic conditions of temperature and relative humidity. The principal advantages are the ability to obtain relatively high concentrations of oxygen efficiently, the cooling of the atmosphere, and the lack of appliances on the patient's face. The disadvantages are its relatively high initial cost, its need for close and constant supervision, and its interference with complete nursing care (71).

Oxygen masks are especially effective for administering very high concentrations of oxygen. There are two types of oxygen-mask apparatus that are considered both comfortable and effective (64).

The oropharyngeal catheter method of administering oxygen is inexpensive and efficient and there is no interference with nursing care.

The positive pressure helmet, also called the helium-oxygen hood, is designed essentially for the administration of helium-oxygen mixtures or 100 percent oxygen.

Loose-fitting masks or face tents consist of plastocele or cardboard coverings which may be molded over the bridge of the nose to include the mouth and nasal openings.

Oxygen chambers and oxygen rooms offer the most comfortable methods of administering oxygen to the patient. A portable oxygen chamber is desirable for use in private residences. The oxygen concentration may be regulated accurately, and nursing and medical care may be carried out with minimal variation in the concentration prescribed.

The various apparatus and methods for the therapeutic administering of oxygen mentioned here are discussed and described in detail by Barach (64).

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